UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

May 21, 2010

MEMORANDUM

SUBJECT: Mutagenicity Hazard Review of PMNs 10-326 [redacted]

FROM: Michael C. Cimino, Ph.D.
Biologist
Science Support Branch
Risk Assessment Division (7403M)

5/21/10

TO: Lemuel T Russell, Ph.D.
Technical Integrator
New Chemical Screening and Assessment Branch (7403M)

THRU: Donald Rodier
Branch Chief
Science Support Branch
Risk Assessment Division (7403M)

5/24/10

10 MAY 25 PM 4:01

RECEIVED

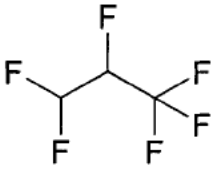
[redacted]

I. CONCLUSION

Based on data on the PMN itself and on analogues, PMN 10-326 is not likely to be a gene mutagen in prokaryotes, nor a chromosome mutation in human cells in culture or in mammals *in vivo*, although it may be a weak chromosome mutagen in nonhuman mammalian cells in culture. Based on data on the PMN itself and on analogues, [redacted]

There is no basis for a mutagenicity concern for these PMNs. No further mutagenicity testing is recommended. This lack of mutagenicity concern does not reduce any concern for carcinogenicity based upon other (non-genotoxicity) data, should such concern exit.

II. STRUCTURES OF P10-326 [redacted]



P10-326

[redacted]

[redacted]

III. BASIS FOR THE CONCLUSIONS

PMNs P10-326 [redacted] identified as Propane, 1,1,2,3,3-hexafluoro- (CAS# 431-63-0) and [redacted], respectively, are illustrated in Section II.. Mutagenicity data were provided for three assays for each of them: a bacterial reverse

mutation assay, a chromosome mutation assay in human cells in culture, and an *in vivo* micronucleus assay in mammals. These data are reviewed below:

Mutagenicity data for P10-326:

I. Bacterial reverse mutation

P10-326 was tested in a bacterial reverse mutation assay, as reported in "Mutagenicity testing of HFC-236ea in the *Salmonella typhimurium* and *Escherichia coli* plate incorporation assay", conducted by [redacted] dated June 30, 1995. The test material (purity 99.983%) was identified as "Propane, 1,1,1,2,3,3-hexafluoro-", with synonyms "HFC 236ea (HFC-236ea)", "Hexafluoropropane" and "1,1,1,2,3,3-Hexafluoropropane", with CAS# 431-63-0. It was tested in *Salmonella typhimurium* strains TA97, TA98, TA100 and TA1535 and *Escherichia coli* strain WP2*uvr*A both without and with metabolic activation using Aroclor 1254-induced Sprague-Dawley rat liver S9. Two independent studies were conducted at five dose levels of 20, 40, 60, 70, 80 and 100% atmospheres, expect that in the second test, due to lack of growth at 100% in the first test, a dose level of 50% was substituted for 100%. Both studies were conducted in triplicate plates. Dose selection was acceptable. The chemical did not induce significant increases in gene mutations under any test condition. Concurrent negative (the diluent, air) and strain- and activation-specific positive controls produced appropriate responses.

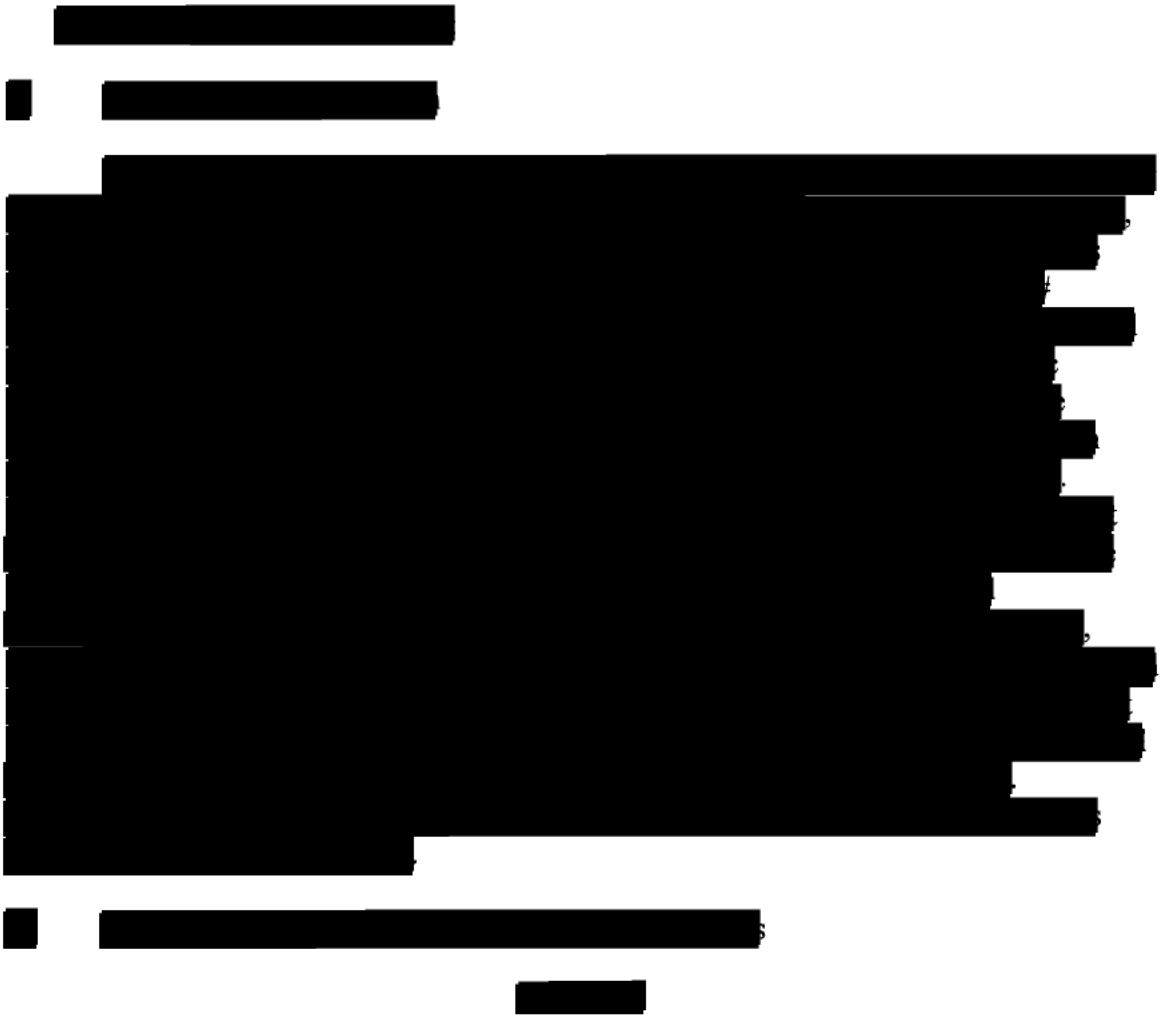
II. *In vitro* chromosome aberration in mammalian cells

The PMN was tested in an *in vitro* mammalian chromosome aberration assay, as reported in "*In vitro* assay of HFC-236ea for chromosome aberrations in human lymphocytes", conducted by [redacted] study dated June 20, 1995. The test material identity and purity were as for the bacterial test above. It was tested in cultured human peripheral blood lymphocytes from one male and one female donor, both without and with metabolic activation as for the bacterial test. Cells were exposed for three hours with 18-19h recovery, without and with activation, to dose levels of 40, 60, 80 and 10% atmospheres. An independent second assay was conducted at the same dose levels. In the second assay an additional harvest time 24h after the first was included for the negative controls and 80% and 100% atmospheres. Cytotoxicity was not observed. Dose selection was acceptable for a noncytotoxic chemical. Duplicate flasks were used for each treatment group, one from the male and one from the female donor. No statistically- or biologically-significant increases in structural aberrations were noted under any treatment condition. Concurrent negative (air) and positive controls (mitomycin C and cyclophosphamide for non-activated and activated assays, respectively) produced appropriate responses.

III. *In vivo* micronucleus assay

The *in vivo* micronucleus study, entitled "Mouse bone marrow micronucleus assay HFC-236ea by inhalation", was conducted by [redacted], study dated June 20, 1995. The test material identity and purity were as for the bacterial test above. The chemical was tested in Crl:CD®-1(ICRI)BR mice by inhalation in whole-body exposure chambers. A rangefinding study determined no toxicity at doses up to 50000ppm, which was the limit that could be applied without oxygen supplementation. No signs of toxicity were observed after dosing. Dose selection was adequate. The mutagenicity assay itself was conducted on five males and five females per treatment group exposed in two 6-hour administrations of the PMN 24 hours apart to dose levels of 5000, 25000 and 50000 ppm, harvested 24 hours and 48 hours after the second exposure. There were no statistically- or biologically-significant increases in micronucleus frequency in any treatment condition in the bone marrow of exposed animals. Concurrent negative (air) and positive (cyclophosphamide) controls showed appropriate responses.

In summary, P10-326 not induce biologically significant increases in gene mutations in prokaryotes, nor chromosome mutation *in vitro* in human cells in culture or *in vivo* in mammalian micronucleus assay under the conditions tested.



[redacted]

[redacted]

The data on the PMNs [redacted] are summarized in the following table:

	Gene mutations			Chromosome mutations		
	SAL	Eco	gm vit	CA vit	MN viv	RDL
[redacted]						
P10-326	neg	neg		HL neg wo & w	neg mouse	
[redacted]						

Abbreviations used in Table:

CA = chromosome aberrations
CHO = Chinese hamster ovary cells
Eco = *Escherichia coli*
gm = gene mutations
HL = human lymphocytes
MN = micronuclei
neg = negative
pos = positive
RDL = rodent dominant lethal
SAL = *Salmonella*
vit = *in vitro*
viv = *in vivo*
wk pos = weak positive

In summary:

Based on data on the PMN itself and on analogues, PMN 10-326 is not likely to be a gene mutagen in prokaryotes, nor a chromosome mutation in human cells in culture or in mammals *in vivo*, although it may be a weak chromosome mutagen in nonhuman mammalian cells in culture.

[redacted]

There is no other basis for a mutagenicity concern for these PMNs. No further mutagenicity testing is recommended. This lack of mutagenicity concern does not reduce any concern for carcinogenicity based upon other (non-genotoxicity) data, should such concern exit.

III. REFERENCES

[redacted]

Kawano, T., Trochimowicz, HJ, Malinverno, G, and Rusch, GM. 1995. Toxicological evaluation of 1,1,1,2,2-pentafluoroethane (HFC-125). Fund Appl Toxicol 28: 223-231 (Abstract only).

NTP. 2010. National Toxicology Program. NTP Database Search Home Page. Online computer database (http://ntp-apps.niehs.nih.gov/ntp_tox), retrieved 05/14/10. National Toxicology Program. Research Triangle Park, NC 27709.